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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,580	06/29/2001	Eric T. Baldwin	6317.N	7868

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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/896,580	Baldwin et al.
Examiner	**Art Unit**
Nashaat T. Nashed	1652

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 29, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above, claim(s) *9-54* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8 and 55-69* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *012502*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1-69 are pending.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I Claims 1-8 and 55-69, drawn to a molecule or molecular complex comprising at least a portion of *S. aureus* peptide deformylase, crystal thereof, and a method making crystal, classified in Class 435, subclass 212.

Group II Claims 9-15, drawn to scalable three-dimensional configuration of point, presumably, a structure defined by the atomic coordinates in Table 1, classified in Class 434, subclasses 365+.

Group III Claims 16 and 17, drawn to a machine-readable data storage medium, classified in Class 360.

Group IV Claim 18, drawn to a method of obtaining structure, classified in Class 702, subclass 22.

Group V Claim 19, drawn to a method of homology modeling, classified in Class 702, subclass 22.

Group VI Claims 20-48, drawn to a method of identifying potential modifier of *S. aureus* peptide deformylase, classified in Class 702, subclass 19.

Group VII Claims 49-51, drawn to a method of making potential modifier of *S. aureus* peptide deformylase, classification is unknown. Since the claims do not identify a specific chemical structure to be made or specific methedology to make the compound, the invention could not be classified because the classification is based on specific chemical structures. For example, a method of making chemical compound utilizing enzymes or organisms are classified in Class 435, subclass 43+. Another example, recombinant method of making peptides and proteins are classified in Class 435, subclass 69.1. Method of chemical synthesis are classified under the class/subclass of a specific chemical compound.

Group VIII Claims 52-54, drawn to a composition comprising a modifier of *S. aureus* peptide deformylase activity, classification is unknown. Since the claims do not identify a specific chemical structure, the invention could not be classified because the classification is based on specific chemical structures.

The inventions are distinct, each from the other because of the following reasons:

The protein molecule or its molecular complexes of Group I, the structure of Group II, the machine of Group III and the methods of Groups IV-VII, and the composition of Group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or

different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions are not disclosed as capable of use together and have different function because:

(a) The invention of Group I is directed to a peptide deformylase which cleaves the amide bond between a formyl group and the N-terminus amino group of a peptide or a protein. In contrast, the invention of Group II is directed to a model of said deformylase which can be used in the methods of Groups IV-VII.

(b) The invention of Group III is directed to a machine-readable data storage medium which is used to construct a three dimensional model of Group II.

(c) The methods of Groups IV-VII do not utilize the molecule or molecular complex of Group I.

(d) The composition of Group I and VIII are independent chemical compounds and would require different searches in the patent and non-patent literature.

The model of Group II, the machine of Group III and the modifiers of Group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different function.

Inventions of Groups II and the methods of Groups IV-VII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the model of Group II is used in the three different methods of Groups IV-VII.

Inventions of Groups III and the methods of Groups IV-VII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the machine of Group III is used in the three different methods of Groups IV-VII.

Inventions of Groups IV-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions are independent methods having different steps and results.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ann Mueting on July 10, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-8 and 55-69. Affirmation of this election must be made by applicant in replying to this Office action. Claims 9-54 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-8 and 55-69 are under consideration in this Office action.

The application has been amended as requested in the communication filed October 9, 2001 and January 11, 2002.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the amino acid sequence contained in Table I is not part of the sequence listing or the computer readable form (CRF), and not identified in the specification with a sequence identification number. In addition, the specification and the claims contain many references to specific amino acid residues presumably from a specific amino acid sequence without identifying the amino acid sequence with a sequence identification number. Applicant must perfect their compliance with the sequence rule.

New formal drawings are required in this application because they are of low quality and contain many informalities, see for example Figure 1. In addition, the Figure descriptions of Figures 15 and 16 contain references to different shade of gray which can not be distinguished in black and white photographs. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

The disclosure is objected to because of the following informalities: The amino acid sequence of SEQ ID NO: 1 is referred to in the specification as deformylase with 6-His tag at the C-terminus, see for example the Figure description of Figure 3. Inspection of SEQ

ID NO: 1 indicates clearly that the N-terminus does not contain 6-His residues at the C-terminus.

Appropriate correction is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see for example page 36, line 10. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Due to the size of the Information Disclosure Statement (IDS) filed on December 12, 2001, the IDS has been separated from the file and appear to be lost. If applicants wish that the examiner consider the references, applicants should refile the references with their response to this Office action. Applicants should feel free to contact the examiner for any assistance.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 55-69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8 and 55-69 are directed to all possible *S. aureus* peptide deformylase, mutants thereof, and the like with the recited characteristics of claim 1, 4 or 7, and crystals thereof as well as method of making crystals. The specification, however, only provides a partial description of a single representative species from *S. aureus* peptide deformylase, i. e., the fusion protein of SEQ ID NO: 1, encompassed by these claims. The specification fails to describe a method of making even the polypeptide of SEQ ID NO: 1 and its conversion to the polypeptide which its structure defined by the atomic coordinates shown in Table 1. It is not clear from the specification what protein molecule has been crystallized or attempted to be crystallized. The atomic coordinates in table 1 describe a

protein containing 184 amino acid ending with Val-His in position 183 and 184, respectively, whereas the amino acid sequence of SEQ ID NO: 1 contains 213 amino acid residues and ending with His-Gln-His-His-His-His at the C-terminus. Also, there is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these *S. aureus* peptide deformylase by any identifying structural characteristics or properties other than those recited in claim 1, 4, and 7 for which no predictability of structure is apparent. While the applicants have taught three different crystals of the same protein, they have not taught any crystals of, presumable, any other mutants other than SEQ ID NO: 1. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 1-8 and 55-69 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a specific mutant of *S. aureus* deformylase identified by a specific sequence identification number, crystal thereof defined by specific space group and unit cell dimensions as well as the angles between the crystallographic axises, and methods of obtaining specific crystals of said deformylase under specific set of crystallization conditions. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible *S. aureus* deformylase and its insertion, deletion, substitution and combination thereof mutants as well as all possible *S. aureus* deformylase-like having similar active site to said deformylase (claims 1-8), crystals thereof and method of obtaining said crystals. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any deformylase derived from *S. aureus* deformylase and include all its possible mutants or any protein having an active site having similar structure to said deformylase. The specification provides guidance and examples in the form of an assay to purify, presumably, the protein of SEQ ID NO: 1 and using said purified protein to obtain several crystals under different crystallization conditions and determine the three dimension structure of the protein using the orthrombic crystal $C222_1$ (see examples). While molecular biological techniques and genetic manipulation to make any protein are known in the prior art and the skill of the artisan are well developed, knowledge regarding crystallization conditions of any *S. aureus*

deformylase or mutants thereof and homolog thereof, crystals that defract X-ray, a specific deformylase mutants that are amenable to crystallization, and metal ions other than divalent Fe, Zn or Ni which are able to bind to the deformylase polypeptide to produce enzymatically active deformylase is lacking. Thus, searching for a molecule or a molecular complex comprising any metal ion of Fe or Ni derived from any *S. aureous* deformylase which can be crystallized is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify a crystallizable mutant(s) of any protein/enzyme is enormous. Since routine experimentation in the art does not include screening vast number of mutants and crystallization conditions where the expectation of obtaining a desired crystal adequate for structure determination by X-ray diffraction is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the primary structure of the protein to be crystallized, the exact crystallization condition, the heavy metal derivatives of the crystal, and the space group and unit cell of the crystal. Without such a guidance, the experimentation left to those skilled in the art is undue. It should be noted that the reagent concentration in the methods claims 55-58 are so broad that one of ordinary skill in the art would have to screen for the appropriate crystallization condition. Changes in crystallization conditions and the primary structure of the protein may result in obtaining different crystals with different structure. Also, one of ordinary skill in the art would doubt the successful crystallization of any metalloprotease such as deformylase at pH around 5 because of the tendency to lose the divalent ion and denaturation of the protein.

Claims 1-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) Claims 1, 3, 4, and 6 contains references to specific amino acid residues from what appears to be a specific amino acid sequence without identifying the amino acid sequence with a sequence identification number which renders the claims indefinite. The numbering of the amino acid residues do not match any sequence in the application including SEQ ID NO: 1. For examination purposes only, it is assumed that those residues numbers are from an amino acid sequence consisting of residues 25-208 of SEQ ID NO: 1.

(b) The phrase "deformylase-like" in claims 1 and 4 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.

(c) The phrase "structurally homologous" in claim 7 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.

(d) Claims 2, 5, and 8 are included in this rejection because they are dependent on a rejected claim and do not cure its deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-8 are rejected under 35 U.S.C. § 102(b) or (e) as being anticipated by Lonetto *et al.* (IDS reference: EP-879979 A2) or U. S. Patent 6,410,688 [(688), Lonetto *et al.*].

Lonetto *et al.* is a published European patent application corresponding to U. S. patent application 08/911,844 which serial number 09/373,953 is a divisional thereof and matured to the 688 patent. Both patent document teach the nucleic acid encoding the peptide deformylase from *S. aureus*, see SEQ ID NO: 1, and the corresponding protein, see SEQ ID NO: 2. The amino acid sequence of SEQ ID NO: 2 taught by Lonetto *et al.* is highly homologous (98.9%) to residues 25-207 of SEQ ID NO: 1 of the instant application. Only two amino acid differed in that region between the two sequences one of which corresponds to the mutation of Arg-127 to Lys. Although both patent document do not teach the structure of the deformylase, its active site residues and the metal ion cofactor required for catalytic activity, the active site residues and their coordinates are intrinsic properties of the deformylase they have taught (claims 1-8).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner